

**Attorney Docket No. 00956.8006.US02  
Application No. 10/550,715**

# **EXHIBIT A**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**APPLICANTS:** Abelardo Silva *et al.*

**CONF. NO.:** 3064

**SERIAL NO.:** 10/550,715

**GROUP NO.:** 1654

**FILING DATE:** August 16, 2006

**EXAMINER:** Roy R. Teller

**TITLE:** *LONG ACTING BIOLOGICALLY ACTIVE CONJUGATES*

**RESPONSE TO THE OFFICE ACTION OF April 28, 2010**

**Mail Stop: Amendment  
Commissioner for Patents  
Randolph Building  
401 Dulany Street  
Alexandria, VA 22314**

Sir:

This is a response to the Office Action mailed April 28, 2010, in the above-captioned application. A response is due October 28, 2010, by virtue of the attached petition for extension of time and payment of the requisite fees. The Commissioner is hereby authorized to charge all fees due for filing this response to Deposit Account No. 50-2283.

In the event that extension of time are required to maintain the pendency of this application at any time during its prosecution, including extension of time beyond those requested in the papers accompanying any response, then such extensions of time are herein petitioned. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

Although Applicants believe the fees submitted with this response are correct, the Commissioner is authorized to charge any additional fees that may be deemed necessary to Attorney's Deposit Account No. 50-2283.

**Amendments to the Claims begin on page 2.**

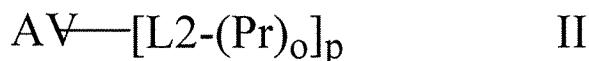
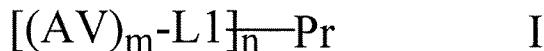
**Remarks begin on page 7.**

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions of claims in the application:

1-17. (Canceled)

18. (Currently Amended) An isolated complex of the Formula I or Formula II:



wherein:

m is an integer from 1-5;

n is an integer from 1-100;

o is an integer from 1-5;

p is an integer from 1-100;

AV is an antiviral compound;

L1 and L2 are polyvalent linkers covalently linking AV to Pr, or where L1 and L2 are absent;

Pr is a protein; and

wherein the complex ~~possesses antiviral activity~~ inhibits HIV in vivo.

19. (Original) The complex of Claim 18, wherein the antiviral compound is a peptide.

20. (Original) The complex of Claim 19 wherein the peptide has a mass of less than about 100 kDA.

21. (Original) The complex of Claim 19, wherein the peptide has a mass of less than about 30 kDA.

22. (Original) The complex of Claim 19, wherein the peptide has a mass of less than about 10 kDA.

23. (Original) The complex of Claim 19 wherein the peptide is a peptidomimetic.

24. (Currently Amended) The complex of Claim 19 wherein the peptide consists of up to 51 amino acids comprising a sequence selected from the group consisting of:

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6**, SEQ ID NO: 843;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7**, SEQ ID NO: 844;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8**, SEQ ID NO: 844;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9**, SEQ ID NO: 846;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10**, SEQ ID NO: 847;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11**, SEQ ID NO: 848;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12**, SEQ ID NO: 849;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13**, SEQ ID NO: 850;

**Y1-X-X-Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14**, SEQ ID NO: 851;

**Y2-X-X-X-Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14**, SEQ ID NO: 852;

**Y3-X-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14**, SEQ ID NO: 852;

**Y4-X-X-Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14**, SEQ ID NO: 854;

**Y5-X-X-Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14**, SEQ ID NO: 855;

**Y6-Y7-X-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14**, SEQ ID NO: 856;

**W-X-X-W-X-X-X-I-X-X-T-X-X-I-X-X-L-I-X-X-Q-X-Q-X-X-N, SEQ ID NO:  
857;**

**W-X1-X2-W-X3-X4-X5-I-X6-X7-X8-T-X9-X10-I-X11-X12-L-I-X13-X14-X15-Q-X16-  
Q-Q-X17-X18-N-X19-X20-X21-X22-X23, SEQ ID NO: [[857]] 858;**  
peptide DP178 (T-20); and  
peptide T-1249;  
wherein:

Y1 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y2 is selected from the group consisting of W, Y, F, H, L, N, Q, E, D, K, and R;

Y3 is selected from the group consisting of I, V, L, A, S and T;

Y4 is selected from the group consisting of T, S, I, K, N, H, R, Q, E and D;

Y5 is selected from the group consisting of I, V, T, K, L, N, Q, D, E, R and H;

Y6 is selected from the group consisting of any amino acid except P, G and C;

Y7 is selected from the group consisting of I, L, V, N, Q, K, R, H, E and D;

Y8 is selected from the group consisting of Q, H, R,N, E, D, K and P;

Y9 is selected from the group consisting of Q, H, N, E, D, K, R, L and P;

Y10 is selected from the group consisting of Q, H, N, E, D, K and R;

Y11 is selected from the group consisting of N, S, T, V, A and D;

Y12 is selected from the group consisting of E, V, K, G, R, Q, D, N, H, T and S;

Y13 is selected from the group consisting of L, I, V, K and R;

Y14 is selected from the group consisting of L, S, M, Y, N, Q, E, D, K, and R;

X1 is selected from the group consisting of M, L, I, Q, T , R and K;

X2 is either E, D, Q and K;

X3 is selected from the group consisting of E, D and K;

X4 is selected from the group consisting of K, R , E, Q, N and T;

X5 is selected from the group consisting of E, L, R, K and Q;

X6 is selected from the group consisting of N, D, S, E, Q, K, R, H, T, I and G;

X7 is selected from the group consisting of N, Q, D, E, K, S, T and Y;

X8 is selected from the group consisting of Y, F, H, I, V and S;

X9 is selected from the group consisting of G, K, R, H, D, E, S, T, N and Q;  
X10 is selected from the group consisting of K, H , E, Q , T, V, I, L, M, A, Y, F, and P;  
X11 is selected from the group consisting of H, K, E, Y and F;  
X12 is selected from the group consisting of T, S, Q, N, E, D, R, K, H, W, G, A, and M;  
X13 is selected from the group consisting of D, E, Q, T , K, R, A, V and G;  
X14 is selected from the group consisting of D, E, K, H, Q, N, S, I, L, V, A and G;  
X15 is selected from the group consisting of S, A and (P);  
X16 is selected from the group consisting of N, K, S, T, D, E, Y, I and V;  
X17 is selected from the group consisting of E, D, N, K, G, and V;  
X18 is selected from the group consisting of K, R, H, D, E, N, Q, T, M, I, and Y;  
X19 is selected from the group consisting of E, V, Q, M , L, J, and G;  
X20 is selected from the group consisting of Q, N, E, K, R, H, L, and F;  
X21 is selected from the group consisting of E, D, N, S, K, A, and G;  
X22 is selected from the group consisting of L, I, and Y; and  
X23 is selected from the group consisting of I, L, M, Q, S, and Y.

25. (Original) The complex of Claim 24 wherein the protein is a blood component.

26. (Original) The complex of Claim 25, wherein the blood component is selected from the group consisting of red blood cells, immunoglobulins, IgM, IgG, serum albumin, transferrin, P90 and P38, ferritin, a steroid binding protein, thyroxin binding protein, and  $\alpha$ -2-macroglobulin.

27. (Original) The complex of Claim 25, wherein the blood component is human serum albumin and the linker is a peptide linker.

28. (Original) The complex of Claim 25, wherein the blood component is human serum albumin and the linker is a non-peptide linker.

29. (Canceled)

30. (Original) The complex of Claim 18, wherein the linker L1 or L2 is a non-labile linker that is stable toward hydrolytic cleavage *in vivo*.

31-145. (Canceled)

## REMARKS

### Claim Amendments

Previously pending Claims 48, 53, 81 and 136-145 are canceled by the accompanying amendment. Claim 18 has been amended to recite that the complex inhibits HIV *in vivo*. Support for this amendment may be found throughout the specification as filed, for example at page 61, lines 24-25. Claim 24 has been amended to insert the definitions of each of amino acid residues Y1 to Y14. The amendment to claim 24 is supported throughout the specification as originally filed, for example at page 49, lines 9-28. Claim 24 also has been amended to insert a missing sequence identifier for sequence No. 857 and to correct a typographical error. No new matter is added by these amendments.

Applicants reserve the right to pursue any subject matter canceled from the claims in one or more continuing applications.

### Provisional Double Patenting over U.S. Patent Application 10/478,811

Applicants respectfully request the provisional non-statutory double patenting rejection be held in abeyance until the scope of patentable subject matter is determined. Moreover, as U.S. Patent Application 10/478,811, has not been allowed, any terminal disclaimer would be premature.

### Rejection of Claims Under 35 U.S.C. § 112, second paragraph

Claim 24 has been amended to address the Examiner's concerns regarding the definition of amino acid residues Y1 to Y14 by inserting the specific recitation of those amino acid residues.

### Rejection of Claims Under 35 U.S.C. § 112, first paragraph

Claims 18-28 and 30 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement, as the specification allegedly "does not reasonably provide enablement for a composition and method for inhibiting antiviral activity *in vivo*." Applicants respectfully disagree with the position taken by the Examiner.

The enablement requirement of § 112 is satisfied when an application describes an invention in a manner that permits one of ordinary skill to practice it without undue experimentation. (MPEP § 2164.01). The Examiner admits that the specification is enabling for compositions and methods for inhibiting the activity of HIV (Office Action at page 4), but

asserts that the specification is not enabled for compositions that possess other antiviral activities *in vivo*. The Examiner does not contend the claimed complexes cannot be made and antiviral assays are known in the art. Conducting antiviral assays requires no more than routine experimentation and nothing the Examiner points to suggests otherwise. Moreover, a patent specification need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

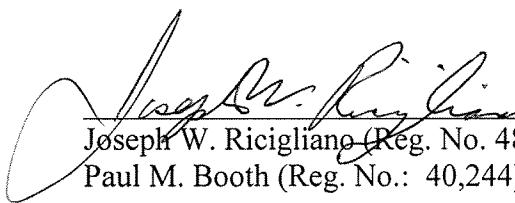
Although Applicants respectfully disagree with the position taken by the Examiner for at least the reasons set forth above, and do not acquiesce to the propriety of the rejection, they have amended the claims to recite that "the complex inhibits HIV *in vivo*", thereby obviating the Examiner's concerns.

### **CONCLUSION**

Applicants respectfully submit that every rejection and objection of the pending claims has been overcome, and they respectfully request withdrawal of those objections and rejections along with an indication that the claims are in condition for allowance. If the Examiner has any questions he is invited to contact Applicants' undersigned representative.

Date: October 28, 2010

Respectfully submitted,



\_\_\_\_\_  
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